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# Status Report on the Uniject™ Prefilled Injection Device

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## Uniject History

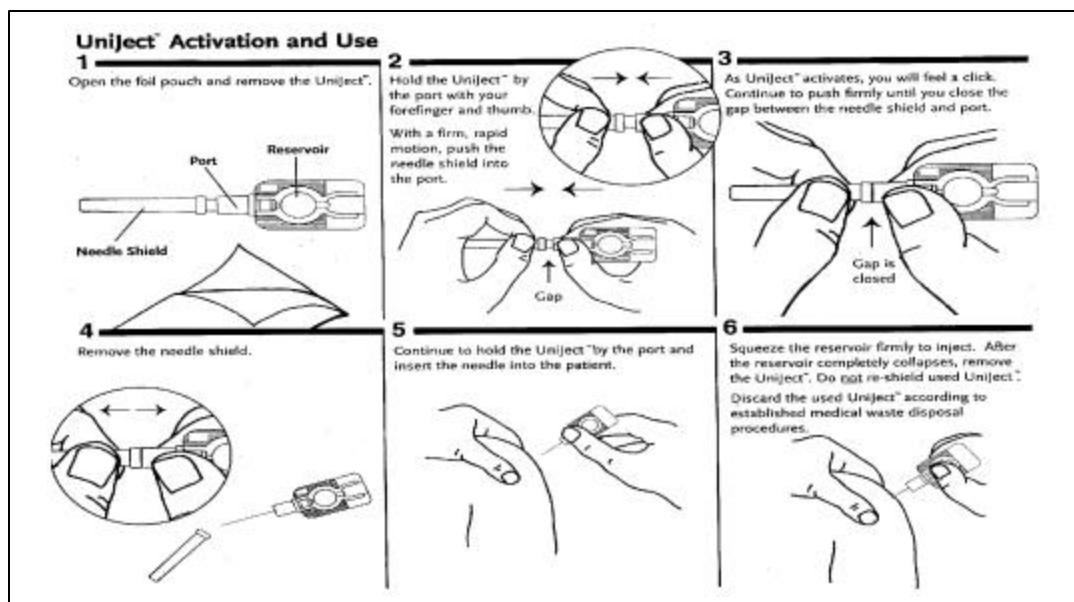
A decade ago, prefilled syringes were too costly for use in public-sector health programs, and no prefilled syringe on the market offered an auto-disable feature. With support primarily from the United States Agency for International Development (USAID) under the Technologies for Health (HealthTech) project, and input and technical assistance from the World Health Organization (WHO) and a multitude of other collaborators, PATH developed a proprietary, auto-disable, prefilled device known as Uniject. Today, the Uniject device is licensed to Becton Dickinson and Company (BD) for commercial production and distribution. This report provides an update to public-sector agencies on the status of Uniject.



Uniject Devices

## Description of Uniject

Uniject is a prefilled, single-dose injection device specifically designed to prevent attempts at reuse. It combines drug or biological, syringe, and needle packaged in a sealed foil pouch. Uniject devices are available in 0.25-, 0.5-, 1.0-, and 2.0-ml dose sizes and can be ordered with any standard needle size.



Uniject Instructions

## Rationale for Uniject

The Uniject device was designed with the following features in mind:

- **Single dose**—to minimize wastage and facilitate outreach to individual patients.
- **Prefilled**—to ensure that the correct dose is given, and to simplify procurement and distribution logistics.
- **Non-reusable**—to minimize patient-to-patient transmission of blood-borne pathogens.
- **Easy-to-use**—to allow self-injection and use by health workers who do not normally give injections, and to facilitate use in emergency situations.
- **Compact size**—for easy transport and disposal.

## Production Status

BD produces Uniject devices in Singapore with a fully automated, high-volume production line and markets them globally to pharmaceutical companies through their regional sales offices.

The process required for a pharmaceutical company to offer a drug or biological in Uniject devices is more complex than one might expect, and usually includes the following steps:

1. identification and characterization of the potential market for the product;
2. pilot fills of the drug or biological into Uniject devices using equipment loaned by BD;
3. compatibility and stability testing of the Uniject/drug combination;
4. clinical or user-acceptability studies (if required by the company or national regulatory authorities);
5. identification and/or design of appropriate processing equipment to fill, seal, inspect, label, and package Uniject devices;
6. purchase, installation, and validation of processing equipment; and
7. completion of regulatory approval processes for the Uniject/drug combination.

From start to finish, the process listed above can be expected to take a minimum of two to three years. Fortunately, at least 37 pharmaceutical companies are well into the process. The targeted drugs include vaccines, injectable contraceptives, uterotonics, and analgesics. Seventeen companies have already conducted pilot fills, and two have purchased processing equipment. The first commercial products in Uniject will become available in 2000. They include hepatitis B vaccine and tetanus toxoid from P.T. BioFarma (Indonesia), and Cycloferm<sup>TM</sup> injectable contraceptive from Aplicaciones Farmacéuticas (Mexico).



**Uniject Production at  
BD Singapore**



**Uniject Packaging Line  
at PT BioFarma**

## Clinical and Field Experience with Uniject

A wealth of experience has been accumulated with Uniject, to date (see Table 1).

**Table 1: Summary of Uniject Studies**

Date	Drug or Biological	Country	Site	Focus
1991-1992	Prostaglandin	Egypt <sup>1</sup>	Hospital	Acceptability
1991	Prostaglandin	India <sup>2</sup>	Hospital	Acceptability
1995	Tetanus toxoid	Bolivia <sup>3</sup>	Homes	Acceptability, use by traditional birth attendants
1995-1996	Tetanus toxoid and hepatitis B vaccine	Indonesia <sup>4,5</sup>	Homes	Acceptability, immunogenicity of hepatitis B vaccine
1995-1996	Cyclofem	Brazil <sup>6</sup>	Clinic	Acceptability
1997	Cyclofem	Brazil <sup>7</sup>	Clinic	Self-administration
1998-2000	Oxytocin	Angola (ongoing)	Hospital	Acceptability
1999-2000	Oxytocin	Indonesia (ongoing)	Homes	Acceptability, use by village midwives
1999-2000	Cyclofem	Mexico (ongoing)	Clinic/Homes	Introduction, self-administration
1999-2000	Hepatitis A vaccine	U.S. (ongoing)	Outpatient clinic	Provider acceptability, clinical equivalence with syringe
2000-2001	Hepatitis B vaccine	Indonesia (planned)	Clinic/Homes	Introduction in two provinces
2001	Hepatitis B vaccine	Philippines (planned)	To be determined	Introduction
2000-2002	Tetanus toxoid	Global (planned)	Outreach	Introduction

The studies occurred with the collaboration of pharmaceutical companies that conducted pilot trials of drugs or biologicals into Uniject and met regulatory requirements to release the products for clinical use. Early studies focused on the acceptability of using Uniject to deliver drugs in difficult situations, e.g., administration of uterotonic drugs to prevent or treat postpartum hemorrhage,<sup>(1,2)</sup> or administration of vaccine to women and children in their homes.<sup>(3,4,5)</sup> In the case of hepatitis B vaccine, the vaccine must be given as close to birth as possible where perinatal transmission is high—meaning that home administration is essential in areas where births take place in the home. A few studies focused on use of Uniject by individuals who do not normally give injections.<sup>(3,7)</sup> Results of studies thus far have revealed the following:

- The Uniject device was found to be easier to use than a standard needle and syringe, and was preferred over a standard needle and syringe.<sup>(2,3,4,6)</sup>
- The activation step,<sup>(2,4,6)</sup> pressure required to collapse the blister,<sup>(6)</sup> and removal of the needle shield<sup>(3)</sup> were found to be difficult by some users using early prototype devices. BD has since improved the device to make these steps easier.
- As with any syringe/needle combination, users must be trained not to recap the needle of the Uniject after use.<sup>(3,4)</sup>
- No significant differences were found in seroconversion rates or geometric mean titers of hepatitis B surface antibody between three groups of infants receiving hepatitis B vaccine stored: (1) in the cold chain and delivered with standard needles and syringes, (2) in the cold

chain in Uniject devices, and (3) at ambient temperatures in Uniject devices for up to one month.<sup>(5)</sup>

- Uniject is highly appropriate for use in outreach programs and for use outside the cold chain.<sup>(3,4)</sup>
- Aspiration is achievable with the Uniject device, but requires specific training.<sup>(6)</sup>
- Individuals who had never delivered an injection are able to successfully do so with Uniject after minimal training.<sup>(3,7)</sup>
- Self-administration of injectable contraceptives using Uniject is a viable option.<sup>(7)</sup>

## **Ongoing Oxytocin-in-Uniject Studies**

Two studies are currently underway in which Uniject is being used to administer oxytocin (ten international units given intramuscularly) to women for routine management of the third stage of labor. The use of oxytocin in this manner can significantly reduce the incidence of postpartum hemorrhage. Both studies are assessing the acceptability of this method to women and health care providers, as well as training and logistical issues. The WHO Safe Motherhood Programme and Karolinska Institute are conducting a study in Angola in which midwives in two maternity units (one central and one peripheral) are using 1,500 oxytocin-filled Uniject devices. WHO/Indonesia and the Indonesian Ministry of Health are conducting a second study in Indonesia. In this study, village-based midwives will use 2,300 oxytocin-filled Uniject devices during home deliveries. Both studies should be complete by April 2000.

## **Uniject Introduction Activities**

Tetanus toxoid, hepatitis B vaccine, and Cyclofem in Uniject are on the verge of wide-scale availability. Introductory studies will be used to pre-test training materials, and distribution and disposal logistics.

### Vaccines

With funding from the Bill and Melinda Gates Children's Vaccine Program, the Ministry of Health will provide three doses of hepatitis B vaccine in Uniject to infants in at least two provinces in Indonesia in 2000. The intention is to expand this method of hepatitis B vaccination nationwide over the next few years. There are also plans to initiate a similar study in one other Asian country, possibly the Philippines.



**Infant Receiving Hepatitis B Vaccine in Uniject (Indonesia)**

The global introduction of tetanus toxoid (TT) in Uniject has been made possible by the five-year (1998-2003) UNICEF/BD tetanus elimination initiative entitled "Partnership for Child Health." BD has donated both a Uniject processing line and nine million Uniject devices to the Partnership. P.T. BioFarma (the national vaccine manufacturer of Indonesia) was identified as the pharmaceutical collaborator via a competitive selection process among UN-qualified vaccine producers and will donate nine million doses of TT for filling into Uniject devices. The processing equipment is currently being installed and validated at P.T. BioFarma. By mid-2000, doses of TT in Uniject (labeled with vaccine vial monitors donated by

LifeLines Technology, Inc.) will begin to flow to countries identified by UNICEF as high risk for maternal and neonatal tetanus. Operational research studies to assess the best integration of tetanus toxoid filled Unijects into immunization programs will be conducted by UNICEF, BASICS, PATH, and local Ministries of Health during 2000 and 2001. The Uniject format is expected to be especially effective in reaching women in small or nomadic populations as well as in areas of conflict.

### Injectable contraceptives

Aplicaciones Farmacéuticas (AF) will commercially launch Cyclofem/Uniject in 2000. In preparation, the three major family planning service providers in Mexico are conducting a comparative survey study to evaluate the acceptability of the product and training materials to 750 women and their health care providers as well as continuity rates over a six-month period (September 1999-February 2000). One-half of the participating women will administer five monthly injections to themselves at home after giving themselves an injection in the clinic under supervision.

### **Uniject Introduction Issues**

A few topics deserve special attention when introducing Uniject into a health program. These include cost-effectiveness, storage capacity, training, and disposal.

#### Cost-effectiveness

A variety of cost factors need to be taken into account when analyzing the appropriateness of Uniject as an injection system for a specific application, including:

- *Cost per dose*—A prefilled Uniject device replaces a vial, syringe, and needle.
- *Wastage reduction*—Savings are likely to be realized when shifting from multi-dose vials to a single-dose format.
- *Transport and storage costs*—Compare costs for shipping and storing Uniject versus current costs for shipping and storing drugs, syringes, and needles. Costs are likely to increase if the drug must be kept in the cold chain and cold chain capacity is inadequate. Programs should be encouraged to identify innovative methods to package and distribute drugs in Uniject to minimize costs. For example, heat-stable vaccines in Uniject could be shipped in insulated containers without refrigeration for certain transport legs. Temperature-monitoring devices (including vaccine vial monitors) can be used to ensure that these procedures do not compromise vaccine quality.
- *Logistics and labor*—The prefilled format simplifies ordering, ensures that a sterile syringe and needle are available with each dose of drug, and minimizes labor costs, e.g., preparation of drugs for injection and syringe sterilization.
- *Safety*—As with other auto-disable syringes, the prevention of patient-to-patient transmission of blood-borne pathogens via syringe and needle reuse or improper sterilization results in long-term savings to health programs.
- *Disposal*—If disposable or auto-disable syringes are currently in use, disposal costs are likely to decrease with Uniject (see Table 2 below). If sterilizable syringes are in use, disposal costs are likely to increase.

**Table 2: Disposal weight comparison for ten 0.5-ml doses  
Uniject versus disposable syringes and vial**

<b>Uniject</b>	<b>Disposable syringes and vial</b>
Ten (0.5-ml) 25G x 5/8" Uniject devices (empty) and ten long foil pouches = <b>29.53 grams</b>	Ten BD 3-cc plastic disposable syringes (empty) + 22 G x 1.5" needle and packaging = 57.40 grams
	One 5-ml glass vial (empty )with rubber stopper and metal cap = 7.51 grams
<b>Total weight = 29.53 grams</b>	<b>Total weight = 64.91 grams</b>

- *Expansion of services*—While difficult to quantify, Uniject can be used in novel ways to increase access to medications. For example, Uniject can facilitate immunization outreach, use beyond the cold chain (especially when vaccine vial monitors are used), home use, self-injection, and use by health workers who do not normally give injections.

### Cold Chain Storage Capacity

For drugs that must be refrigerated, volume estimates must be made to see if current cold chain storage capacity is adequate to accommodate a move to a single-dose format. In the case of vaccines, a move to multivalent vaccine may offset the increased storage requirements for the single-dose format. Increased distribution schedules can also sometimes decrease storage capacity requirements at peripheral facilities.

The size of a prefilled Uniject device will vary depending upon the volume of drug it holds, the needle size, and the outer packaging. For example, a box of 1,500 filled Uniject devices (0.5-ml, 25-gauge x 5/8" needle) in foil pouches has a volume of approximately 0.091 cubic meters or 3.22 cubic feet.

### Training

Experience has shown that training health personnel in Uniject use is a fairly uncomplicated and brief process. Health worker training can be accomplished within one to two hours. The training can include instruction on proper use and disposal of Uniject, review of safe injection procedures, and practice with the device.

Certain issues require reinforcement during training. These include:

- Activation step to open flow from drug reservoir
- Hand placement to avoid accidental expulsion of the drug
- Proper injection at a downward angle
- Aspiration, where practiced
- Prevention of recapping

### Disposal

If not already in place, it is important to plan for an effective disposal system before Uniject devices are introduced. One benefit of Uniject is that it contains only about 35 percent of the amount of plastic of a standard disposable syringe. It weighs significantly less than a disposable



syringe and single-dose vial. The plastics used in Uniject can be incinerated without the generation of toxic fumes, such as those produced by the rubber piston in standard disposable syringes. When incinerated, the basic ingredients of polymers of carbon, hydrogen, and oxygen result in conversion to water and carbon dioxide. These materials can usually be safely discharged into the atmosphere.

In instances where Uniject devices are used for outreach, it is recommended that health workers transport and store devices in a protective outreach carrier. In Uniject studies, PATH has used a small plastic box for this purpose (see photo). The carrier has a strap for easy carrying and a latch to keep the carrier securely closed.



**Uniject Outreach Carrier**

The outreach carrier contains a compartment that holds 30 Unijects in foil pouches and a compartment that holds a removable cardboard disposal box. The disposal box accepts up to 50 used Unijects. To prevent access to the used syringes, the disposal box is permanently sealed, and the insertion hole is designed to prevent contaminated needles from protruding. At regular intervals, the cardboard disposal box is removed, incinerated, and replaced with a new box. At the same time, the health worker can receive a new supply of filled Unijects. Programs may wish to develop similar containers and procure them locally.

## **The Future of Uniject**

The full potential of Uniject in public health programs has yet to be realized. Some of the most exciting and presumably cost-effective applications such as use with new, expensive, and/or multivalent vaccines remain to be tested. The new Global Alliance for Vaccines and Immunization has resolved to promote the use of vaccine combinations and mono-dose delivery devices that facilitate outreach. Such interest may accelerate the availability of new vaccines in Uniject via the creation of a powerful public-sector market force. The possibility of modifying Uniject into a dual chamber device that can be used to deliver lyophilized drugs is being analyzed by the USAID-supported HealthTech project and BD, as one of many options to improve the safety and handling of reconstituted vaccine. USAID is also supporting efforts to make the injectable contraceptive Depot Medroxy Progesterone Acetate (DMPA) available in Uniject and to investigate the use of the device to deliver gentamicin for presumptive early treatment of infant infections. The combination of these efforts and the commercial efforts of BD should ensure broad-scale availability of a variety of important drugs and vaccines in Uniject to the public sector.

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